I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: April 6, 2006 Signature: _____ (Jeffrey S. Sharp)

Docket No. 29853/37706
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Shuyuan ZHANG et al.

Application No.: 10/033,491 Confirmation No.: 9920

Filed: December 27, 2001 Art Unit: 1632

For: METHOD FOR TREATING PATIENTS WITH ADENOVIRAL VECTORS Examiner: Robert M. Kelly

DECLARATION OF KERSTIN B. MENANDER, PH.D., M.D. UNDER 37 C.F.R. 1.132

I, Kerstin Menander, declare that:

1. I am the Vice President of Clinical Development at Introgen Therapeutics, Inc. ("Introgen"), assignee of the above-captioned application. I have been employed at Introgen since 2002. As evidenced by my attached *curriculum vitae* (see Exhibit 1), I have broad experience in the health care field in the pharmaceutical, scientific, regulatory and medical arenas. I received a Medical Degree and completed a Ph.D. in Histology (*cum laude*) at the University of Lund in Sweden. I have expertise in the management of all phases of clinical trials with emphasis on oncology, rheumatology and other inflammatory diseases. I have served in senior level management positions with Syntex, Abbott and several smaller biotech companies such as Collagen Corporation and Cell Pathways Inc. where I was responsible for Clinical and Regulatory management of the strategy for the development of drugs, biologics and devices as well as the management of the clinical trials groups responsible for the execution of studies. I have interacted with regulatory agencies in the U.S., Canada and

cancer, glioma, prostate cancer, head and neck cancer, bladder cancer, ovarian cancer, colorectal cancer, malignant ascites, melanoma and solid tumors from a variety of origins.[1]

4. Several clinical trials have been conducted for various cancers including ovarian cancer, lung cancer, bladder cancer, and metastatic colorectal cancer using a different Ad-p53 construct from another company, Schering Plough.[2]

5. The clinical trials discussed in paragraphs 3 and 4 involved or will involve a variety of administrations of Ad-p53 constructs. Administrations include: intraperitoneal, intravenous, intravesical, intratumoral, intramucosal injection, oral rinse, and broncho-alveolar lavage.

6. I anticipate Introgen will proceed with other clinical trials in the future involving adenovirus-p53 constructs, given the success I have observed in the ongoing or previous clinical trials with Introgen's product, INGN 201.

7. In addition to clinical trials directed to cancer treatment numerous workers in the field are conducting clinical trials directed to a variety of other disease states utilizing adenovirus vectors. A recent search for U.S.-based clinical trials utilizing adenoviral vectors yielded 189 adenovirus-based clinical trials. (Exhibit 3) In addition to trials for cancer, clinical trials are reported to be currently underway for treatment of cystic fibrosis, partial ornithine transcarbamylase deficiency, Canavan Disease, Peripheral Vascular Disease, Critical Limb Ischemia, Diabetic Ulcers, Coronary Artery Disease, Peripheral Arterial

[1] *See*, e.g., Swisher *et al.* (2000); Shimada *et al.* (2002); Wolf *et al.* (2004); Pagliara *et al.* (2003); Clayman *et al.* (1999); Swisher *et al.* (1999); Nemunaitis *et al.* (2000); Pisters *et al.* (2004); Lang *et al.* (2003); Kubba *et al.* (2000); Weill *et al.* (2000); Introgen Media Release (05/14/2001); Introgen Media Release (05/17/1999); Introgen Media Release (11/19/2003); and Biotechnology Law Report (June, 2004) (Exhibit 3).

[2] *See, e.g.*, Barnard (2000); Horowitz (1999); Kuball *et al.* (2002); Schuler *et al.* (2001); Buller *et al.* (2002); Dummer (2000); and the reference of Wills *et al.*, which provides the details regarding the structure of the SCH 58500 Ad-p53 construct, which lacks protein IX. (Exhibit 4).

Occlusive Disease, Hemophilia, Treatment of Dialysis Patients, and Parkinson's Disease. (Exhibit 3)

8. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under § 1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this patent, and any reexamination certificate issuing thereon.

APRIL 5, 2005
Date

Kerstin B. Menander, Ph.D., M.D.

Curriculum Vitae

Kerstin B. Menander, M.D., Ph.D.
Telephone: (713-665-9058)
(713) 610-4075

Born: Karlshamn, Sweden

Personal: Two adult children

Education and Degrees:

1972 M.D.; University of Lund, Lund, Sweden

1970 Registrar; University of Lund, Lund, Sweden

1969 Ph.D. Histology (cum laude); University of Lund, Lund, Sweden

1958 H.S. and Junior College (magna cum laude) Lund, Sweden

1955 Senior H.S.; Billings, Montana

Industrial Appointments:

2002 – present	Vice President, Clinical Development Introgen Therapeutics, Inc, Houston, Texas
2000 – 2002	Vice President, International Operations, Cell Pathways, Inc.
1998 – 2000	Vice President, Medical and Regulatory Affairs, Cell Pathways, Inc.
1997 – 1998	Vice President, Medical Affairs Cell Pathways, Inc., Horsham, Pennsylvania
1992 – 1994	Corporate Vice President, Medical Affairs Curative Technologies, Inc. East Setauket, New York
1989 – 1998	President

	US 3 D Development, Inc. San Francisco, California
1986 - 1989	Corporate Vice President Medical and Regulatory Affairs Collagen Corporation Palo Alto, California
1984 – 1986	Medical Director, Clinical Development (included significant Regulatory Affairs responsibilities) Abbott Laboratories Pharmaceutical Products Division North Chicago, Illinois
1985 – 1986	Product Manager, Marketing Abbott Laboratories
1980 – 1984	Director, Clinical Investigation Syntex Laboratories Syntex, Inc. Palo Alto, California
1976 – 1979	Corporate Vice President, Director Medical Affairs Diagnostic Data, Inc. Mountain View, California
1974 – 1976	Corporate Vice President, Regulatory Affairs Diagnostic Data, Inc. Mountain View, California
1973 – 1974	Director, Medical and Regulatory Affairs Diagnostic Data, Inc. Mountain View, California
1970 – 1973	Project Manager, Medical Department AB Leo Halsingborg, Sweden

University Appointments:

Appointments held at the Department of Histology, University of Lund, Sweden:

1969 – 1970	Associate Professor

1962 – 1969	Lecturer
1960 – 1962	Assistant Lecturer

School for Nurses, Lund, Sweden:

1966 – 1970	Lecturer, Anatomy and Physiology

Memberships:

1999 American Gastroenterological Association
1988 Regulatory Affairs Professionals Society
1985 American Heart Association
1984 Drug Information Association
1982 American Society of Clinical Pharmacology and Therapeutics
1982 American Pain Society
1982 American Association for the Advancement of Science
1982 American Association for the Study of Headache
1981 Society for Clinical Trials
1980 Fellow, Royal Society of Medicine
1977 American College of Rheumatology
1976 Society for Experimental Biology and Medicine
1976 New York Academy of Sciences
1965 Society for Fertility and Sterility

Miscellaneous Other Facts of Interest:

1989	Co-chaired sessions on Biotechnology and Regulatory Affairs, Annual Meeting, 1989, Drug InformationAssociation
1989	Selected as one of 2,000 Notable Women
1985 – 1986	Chairman, Scientific Affairs Committee National Pharmaceutical Council
1981 – 1986	Member, Scientific Affairs Committee National Pharmaceutical Council
1954 – 1955	American Field Service Scholarship to the U.S.

1954 Scholarship, Royal Foundation for the Promotion of Swedish Culture Abroad

Scope of Experience:

Clinical Trials:
(Phases I, II and III):

Clinical Studies in all phases of drug development. Considerable experience in Phases I, II and III. Managed the execution of and/or performed trials especially in oncology with proapoptotic drugs, rheumatoid arthritis and other inflammatory diseases. Additionally in endocrinology (estrogen replacement therapy and osteoporosis prevention, oral contraceptives), orthopedics, allergology, analgesiology, cardiovascular conditions, infectious diseases, wound healing, neurology, and dermatology. Managed pharmacokinetic unit.

(Phase IV Activities):

Managed groups responsible for Clinical Trials, Adverse Reaction and Medical Information Departments.

Basic Research:

Conducted independent research in histology, endocrinology and in the area of inflammation.

Patents:

Have several patents granted in my name.

Regulatory Experience:

Developed regulatory strategies for dealing with the regulatory agencies as well as for the development of different health care products.

Interacted with regulatory agencies in the U.S. (drugs, biologics and devices), Canada and Europe. In addition, managed regulatory departments responsible for assembly, submission and approval of IND's, IDE's, NDA's, PLA's, PMA's. Responsible for final clinical and regulatory approval of promotional materials and for package inserts.

The positions at Syntex and Abbott included frequent FDA contacts, as well as regulatory responsibilities)

International and Domestic Contacts:

Have extensive contacts within the drug industry and the medical, scientific community in the U.S., Europe and Japan. During the last six or seven years interacted with many opinion leaders within the oncology community.

Health Care Policies:

Dealt with health care policies as a member and Operating Chairman of the Scientific Affairs Committee of the National Pharmaceutical Council. Have also been involved in cost benefit studies as well as reimbursement issues.

New Business and Licensing:

Have regularly evaluated potential acquisitions and have throughout my career acted as a liaison in licensing negotiations.

As Vice President, International Operations I have established contacts with different major global, European and Japanese companies for the purpose of creating marketing alliances. In addition, I have been part of the development of the terms as well as participated in the negotiations.

Strategic Planning:

Was an integral part in the strategic planning process within several therapeutic areas as well as in the development of strategies for how industry can meet the challenges of a changing health care system

Business:

Have participated as a Corporate Officer in top management discussions and decisions.

Marketing:

Functioned as a Product Manager and was responsible for developing a marketing as well as a launch, production and manufacturing plan.

Strengths:

Broad experience in the health care field; broad pharmaceutical, scientific, regulatory and medical experience. In addition, analytical, creative, energetic, interactive team player; leadership. Extensive experience in major pharmaceutical companies as well as in start-ups.

PUBLICATIONS

1. Falck, B., Nordanstedt, O., Menander, K., Intra-ovarian Mechanisms in HCG-Induced Oestrogen Secretion. Lund Universities Aerskrift. N.F. Art. 2, Vol. 56, No. 15, 1960.

2. Falck, B., Nordanstedt, O., Menander, K., Androgen Secretion by the Rat Ovary. Nature, Vol. 93, No. 4815, 593-594, February 10, 1962.

3. Menander-Sellman, K., Secretion of Gonadotrophic hormones by Hypophyseal Transplants in the Rat. Acta Universitatis Lundensis, Section II, 1964, No. 2, 1-12.

4. Menander-Sellman K., The Structure of Oestrogen Sensitized Rat Vagina after Exposure to Steroids as Studies in Transplants. Z. Zellforsch, 100, 83-92, 1969.

5. Menander-Sellman K., The Luteinization of Granulosa Cells in Rats – Its Dependence of Steroids and Gonadotrophins. In "A Study of the Corpus Luteum Cells and the Granulosa Cells of the Rat in Vivo in Microtransplants." (1969) Lund.

6. Menander-Sellman, K., In Vivo Production of Gestagens in Corpus Luteum Cells and in Luteinized Granulosa Cells in the Rat. In "A Study of the Corpus Luteum Cells and the Granulosa Cells of the Rat in Vivo in Microtransplants." (1969) Lund.

7. Menander-Sellman, K., Effect of Prolactin on Corpus Luteum Cells of the Rat Ovary in Vivo. In "A Study of the Corpus Luteum Cells and the Granulosa Cells of the Rat in Vivo in Microtransplants." (1969) Lund.

8. Menander-Sellman, K., The Granulosa Cell – Corpus Luteum Cell System, Its Dependence on the Pituitary and its Secretion of Gestagens. Thesis: Univeristy of Lund, 1969.

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11. Thorngren, K.G., Hansson, L.I., Stenström A., Menander-Sellman, K., Effectg of Dose and Administration Period of Growth Hormone on Longitudinal Bone Growth in Hypophysectomized Rats. Acta Endocr. 74, 1-23, 1973b.

12. Lima deFaria, A., Ghatneker, R., Menander, K.B., Development of Human Meiosis in Vitro. Hereditas, 78, 265-272 (1974).

13. Lund-Oleson, K., Menander, K.B., Orgotein: A New Anti-inflammatory Metalloprotein Drug: Preliminary Evaluation of Clinical Efficacy and Safety in Degenerative Joint Disease. Curr. Ther. Res. 16(7), 706-717 (1974).

14. Marberger, H., Bartsch, G., Huber, W., Schulte, T.L., Menander, K.B., Orgotein: A New Drug for the Treatment of Radiation Cystitis. Current Therapeutc Research, 18(3), 466-475, 1975.

15. Edsmyr, F., Menander, K.B., Huber, W., Orgotein Efficacy in Ameliorating Side-Effects Due to Radiation Therapy. I. Double-Blind, Placebo-Controlled Trial in Patients with Bladder Tumors. Current Therapeutic Research, 19, 198-211, 1976.

16. Menander, K.B., Orgotein: A New Anti-Inflammatory – Clinical Use to Data. Invited Lecturer, Scientific Conferences, Karolinska Hospital, Stockholm, Sweden, 11 February 1977.

17. Menander, K.B., Edsmyr, F., Huber, W., Orgotein (Superoxide Dismutase): A Drug for the Amelioration of Radiation-Induced Side Effects. Invited lecturer, WHO Center Meeting on Urinary Bladder Carcinoma, Stockholm, 18-2, April 1977. Published in Urological Research 6(4), 1978.

18. Lund-Oleson, K., Menander-Huber, K.B., Intra-Articular Orgotein Therapy in Osteoarthritis: A Double-Blind, Placebo-Controlled Trial, XIV Inter-national Congress on Rheumatology, San Francisco, CA, June 26-July 1; Abstract #892.

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20. Menander-Huber, K.B., Huber, W., Orgotein: The Drub Version of Bovine Cu-Zn Superoxide Dismutase: II. A Summary Account of Clinical Trials in Man and Animals. In "Superoxide Dismutases", Ed. A.M. Michelson, J. Mcord, and I. Fridovich, Academic Press, London, 537-549 (1977).

21. Huber, W., Menander-Huber, K.B., Saifer, M.G.P., Dang, P.H-C., Studies on the Clinical and Laboratory Pharmacology of Drug Formulations of Cu-Zn Superoxide Dismutases (Orgotein), Perspectives of Inflammation – Future Trends and Developments. Ed. D.A. Willoughby, J.P. Giroud, and G.P. Velo. University Press, Baltimore, 527-617 (Feb. 14-18, 1977).

22. Edsmyr, F., Menander-Huber, K.B., Huber, W., Orgotein Efficacy in Ameliorating Side-Effects Due to Radiation Therapy. Double-Blind, Placebo-Controlled Trials in Patients with Bladder and Prostate Tumors. Presented at the 20th Annual Scientific Meeting of the American Society of Therapeutic Radiologists, Los Angeles, CA, Oct. 31 – Nov. 4, 1978.

23. Edsmyr, F., Menander-Huber, K.B., Huber, W., Orgotein Efficacy in Ameliorating Side Effects Due to Radiation Therapy. Double-Blind, Placebo-Controlled Trials in Patients with Bladder and Prostate Tumors. Invited presentation at meeting on Urological Oncology: Bladder Tumors. Sponsored by the European Urological Association, the WHO Collaborating Center for Research and Treatment of Urinary Bladder Cancer, European Organization of Research on the Treatment of Cancer (EORTC). Sicily, Nov. 3-8, 1978.

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25. Edsmyr, F., Menander-Huber, K.B., Huber, W., Orgotein Efficacy in Ameliorating Due to Radiation Therapy, Proc. Symp. Active Oxygen and Medicine, Honolulu, Hawaii, 1 February 1979, in publication by Raven Press, New York, U.S.A.

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Table of Adenovirus-p53 Clinical Trials (as of December 2004)

Treatment	Cancer	Admin	Clinical Stage	Status/Result (citation)
INGN 201	SCCHN (T301)	Intratumoral	III	Ongoing (1)
INGN 201	SCCHN (T302)	Intratumoral (with chemotherapy)	III	Ongoing (1)
INGN 201	NSCLC	Intratumoral (with radiation therapy)	II	Combination INGN 201 and radiation therapy appears more effective than radiation alone. (2)
INGN 201	SCCHN (T207)	Intratumoral	II	Safe
INGN201	Locally advanced primary breast	Intratumoral (with chemotherapy)	II	Study has been initiated
INGN 201	Esophageal	Intratumoral	I/II	Safe; Ongoing (3)
INGN 201	SCCHN (T201)	Intratumoral	II	Safe; demonstrated clinical activity (4)
INGN 201	SCCHN (T202)	Intratumoral (lower dose)	II	Safe; trend towards shorter survival than T201 (4)
INGN 201	Ovarian	Intraperitoneal	I	Transgene expression observed and increased expression of downstream marker; well-tolerated. (5)
INGN 201	Ovarian	Intraperitoneal (laparoscopy)	I	Well-tolerated; potentially useful clinical response. (5)
INGN 201	Bladder	Intravesical	I	Transgene expression observed; safe (6)

INGN 201	Advanced solid tumors (colon, breast, prostate, sarcoma, NSCLC, H&N)	Intravenous	I	Well tolerated at doses up to $1x10^{12}$ vp; accrual is ongoing to further determine MTD; evaluation of p53 expression is pending
INGN 201	SCCHN	Intratumoral (with and without tumor resection)	I	Transgene expression and expression of downstream targets observed; safe; potentially useful clinical response (7)
INGN 201	NSCLC	Intratumoral	I	Transgene expression and apoptosis observed; safe; potentially useful clinical response (8)
INGN 201	NSCLC	Intratumoral (with cisplatin)	I	Expression observed; well tolerated; potentially useful clinical response (9)
INGN 201	Prostate	Intratumoral (INGN 201 treatment prior to tumor resection)	I	Transgene expression and apoptosis demonstrated; safe (10)
INGN 201	Glioma	Intratumoral and intracranial (stereotactic injection intratumorally, followed by tumor resection, followed by injection into tumor bed	I	Study closed; Expression observed; safe; apoptosis observed (11)
INGN 201	Hepatocellular Carcinoma	Intratumoral	I	Study closed; 1 patient treated

INGN 201	Breast	Intratumoral (with chemotherapy)	I	Study closed; 2 patients treated
INGN 201	Bronchioloalveolar lung carcinoma	Broncho-alveolar lavage	I	Safe; potentially useful clinical response; ongoing (12)
INGN 201	Malignant ascites	Intraperitoneal	I	Study closed; 1 patient treated
INGN 201	Colorectal	Intratumoral	I	Study closed; 6 patients treated; expression of downstream markers demonstrated
INGN 201	Lung	Intratumoral (with and without cisplatin)	I	Study closed; 12 patients treated; potentially useful clinical response (13)
INGN 201	Oral dysplasia (premalignant)	Intramucosal injection; oral rinse	I/II	Ongoing (14)
SCH 58500	Ovarian	Intraperitoneal (with chemotherapy)	II/III	Reported closed
SCH 58500	Lung	Intratumoral (with chemotherapy)	II	Transgene expression observed; well-tolerated; enhanced local effects suggested with certain chemotherapies (15)
SCH 58500	Ovarian	Intraperitoneal (with chemotherapy)	I/II	Well tolerated; expression observed; prolonged patient survival (16)
INGN 201	Melanoma	Intratumoral (with chemotherapy)	I	Transgene expression; Safe(17)

SCH 58500	Lung	Intratumoral	I	Transgene expression and expression of downstream target observed; safe; transient tumor growth control. (18)
SCH 58500	Bladder	Intratumoral or intravesical (with transduction enhancer)	I	Transgene expression and expression of downstream marker demonstrated after intravesical instillation. (19)

* The Chinese State Food and Drug Administration announced in January of 2004 that an Adenovirus-p53 vector, produced by Shenzhen SiBiono GeneTech Co., Ltd., has been granted marketing approval as a cancer treatment (20). We understand that this Adenovirus-p53 vector expresses p53 from the viral RSV promoter.

The Journal of Gene Medicine

Gene Therapy Clinical Trials Worldwide

Provided by the Journal of Gene Medicine

Displaying records **1** through **10** of **189** records found

Trial ID	Title
US-034	A Phase I Study, in Cystic Fibrosis Patients, of the Safety, Toxicity, and Biological Efficacy of a Single Administration of a Replication Deficient, Recombinant Adenovirus Carrying the cDNA of the Normal Human Cystic Fibrosis Transmembrane Conductance Regulator Gene in the Lung
US-035	Gene Therapy of Cystic Fibrosis Lung Diseases Using E1 Deleted Adenoviruses: A Phase I Trial
US-036	Cystic Fibrosis Gene Therapy Using an Adenovirus Vector: In Vivo Safety and Efficacy in Nasal Epithelium
US-041	A Phase I Study of Gene Therapy of Cystic Fibrosis Utilizing a Replication Deficient Recombinant Adenovirus Vector to Deliver the Human Cystic Fibrosis Transmembrane Conductance Regulator cDNA to the Airways
US-042	Gene Therapy for Cystic Fibrosis Using E1 Deleted Adenovirus: A Phase I Trial in the Nasal Cavity
US-067	Adenovirus-Mediated Gene Transfer of CFTR to the Nasal Epithelium and Maxillary Sinus of Patients with Cystic Fibrosis
US-079	Clinical Protocol for Modification of Tumor Suppressor Gene Expression and Induction of Apoptosis in Non-Small Cell Lung Cancer (NSCLC) with an Adenovirus Vector Expressing Wildtype p53 and Cisplatin
US-085	Evaluation of Repeat Administration of a Replication Deficient, Recombinant Adenovirus Containing the Normal Cystic Fibrosis Transmembrane Conductance Regulator cDNA to the Airways of Individuals with Cystic Fibrosis
US-089	Treatment of Advanced CNS Malignancy with the Recombinant Adenovirus H5.020RSVTK: A Phase I Trial
US-090	Treatment of Advanced Mesothelioma with the Recombinant Adenovirus H5.010RSVTK: A Phase I Trial

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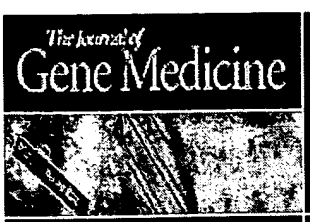


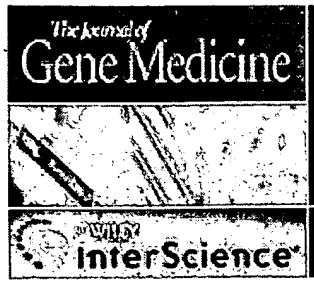
Gene Therapy Clinical Trials Worldwide

Provided by the Journal of Gene Medicine

Displaying records **11** through **20** of **189** records found

Trial ID	Title
US-091	Adenovirus Mediated Gene Transfer for Cystic Fibrosis: Safety of Single Administration in the Lung (lobar instillation)
US-094	Adenovirus Mediated Gene Transfer for Cystic Fibrosis: Safety of a Single Administration in the Lung (aerosol administration)
US-096	Clinical Protocol for Modification of Tumor Suppressor Gene Expression in Head and Neck Squamous Cell Carcinoma (HNSCC) with an Adenovirus Vector Expressing Wild-type p53
US-097	Gene Therapy of Primary and Metastatic Malignant Tumors of the Liver Using ACN53 Via Hepatic Artery Infusion: A Phase I Study
US-098	Phase I Study of Adenoviral Vector Delivery of the HSV-TK Gene and the Intravenous Administration of Ganciclovir in Adults with Malignant Tumors of the Central Nervous System
US-124	A Phase I Study of Recombinant Adenovirus Vector-Mediated Delivery of an Anti-erbB-2 Single Chain (sFv) Antibody Gene for Previously Treated Ovarian and Extraovarian Cancer Patients
US-125	A Phase I Study of Direct Administration of a Replication-Deficient Adenovirus Vector Containing the E. coli Cytosine Deaminase Gene to Metastatic Colon Carcinoma of the Liver in Association with the Oral Administration of the Pro-Drug 5-Fluorocytosine
US-133	Phase I Study of Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector
US-135	A Phase I Study of Recombinant Adenovirus Vector-Mediated Intraperitoneal Delivery of Herpes Simplex Virus Thymidine Kinase (HSV-TK) Gene and Intravenous Ganciclovir for Previously Treated Ovarian and Extraovarian Cancer Patients
US-139	A Phase I Study of Adenoviral Vector Mediated Gene Transfer to Liver in Adults with Partial Ornithine Transcarbamylase Deficiency

Previous Page New Search Next Page



Gene Therapy Clinical Trials Worldwide

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Displaying records **21** through **30** of **189** records found

Trial ID	Title
US-140	Phase I Trial in Patients with Metastatic Melanoma of Immunization with a Recombinant Adenovirus Encoding the MART-1 Melanoma Antigen
US-144	Phase I Study of Adenoviral Vector Delivery of the HSV-tk Gene and the Intravenous Administration of Ganciclovir in Men with Local Recurrence of Prostate Cancer after Radiation Therapy
US-145	Gene Therapy of Bladder Cancer Using Recombinant Adenovirus Containing the Retinoblastoma Gene (ACNRB): A Phase IA Study
US-148	Phase I Study of Adenoviral Vector Delivery of the HSV-tk Gene and the Intravenous Administration of Ganciclovir in Adults with Recurrent or Persistent Head and Neck Cancer
US-151	Phase I Trial in Patients with Metastatic Melanoma of Immunization with a Recombinant Fowlpox Virus Encoding the GP100 Melanoma Antigen
US-164	Phase I Trial of Adenoviral Vector Delivery of the Herpes Simplex Thymidine Kinase Gene by Intratumoral Injection Followed by Intravenous Ganciclovir in Patients with Hepatic Metastases
US-165	Phase I Trial In Patients With Metastatic Melanoma Of Immunization With A Recombinant Fowlpox Virus Encoding the GP100 Melanoma Antigen
US-171	Immune Response to Intradermal Administration of an Adenovirus Type 5 Gene Transfer Vector (AdGVCD.10) in Normal Individuals
US-175	Gene Therapy for Recurrent Glioblastoma Multiforme: Phase I Trial of Intraparenchymal Adenoviral Vector Delibvery of the HSV-TK Gene and Intravenous Administration of Ganciclovir
US-187	Phase I Trial of Adenoviral-Mediated Herpes Simplex Thymidine Kinase Gene Transduction in Conjuction with Ganciclovir Therapy as Neo-adjuvant Treatment for Patients with Clinically Localized (Stage T1c and T2b&c) Prostate Cancer Prior to Radical Prostatectomy

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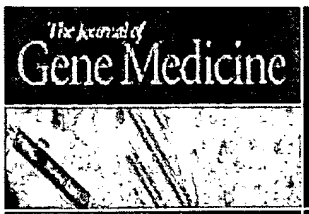

Gene Therapy Clinical Trials Worldwide

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Displaying records **31** through **40** of **189** records found

Trial ID	Title
US-189	Phase I Study of Percutaneous Injections of Adenovirus p53 Construct (Adeno-p53) for Hepatocellular Carcinoma
US-192	A Phase I Study in Patients with Locally Advanced or Recurrent Adenocarcinoma of the Prostate Using SCH58500 (rAd/p53) Administered by Intratumoral Injection
US-202	A Phase I Study of Vaccination with Autologous, Lethally Irradiated Melanoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor
US-203	A Phase I Study of Vaccination with Autologous, Lethally Irradiated Non-Small Cell Lung Carcinoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor
US-209	Systemic and Respiratory Immune Response to Administration of an Adenovirus Type 5 Gene Transfer Vector (AdGVCD.10)
US-211	Gene Therapy of Canavan Disease: Retreatment of Previously Treated Children
US-214	A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)
US-216	Phase I/Pilot Study of p53 Intralesional Gene Therapy with Chemotherapy in Breast Cancer
US-217	A Tolerance and Efficacy Study of Intraprostatic INGN 201 Followed by Pathological Staging and Possible Radical Prostatectomy in Patients with Locally Advanced Prostate Cancer
US-219	A Phase I Trial of Intravesical Ad-p53 Treatment in Locally Advanced and Metastatic Bladder Cancer

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Gene Therapy Clinical Trials Worldwide

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Displaying records **41** through **50** of **189** records found

Trial ID	Title
US-220	A Phase II Gene Therapy Study in Patients with Non-Small Cell Lung Cancer Using SCH 58500 (rAd/p53) in Combination with Chemotherapy for Multiple Cycles
US-221	Phase I Study of Direct Administration of a Replication-Deficient Adenovirus Vector (AdGVVEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Life Threatening Diffuse Coronary Artery Disease
US-222	Gene Therapy in Patients with Canavan Disease
US-224	Phase I Study of Chemokine and Cytokine Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma Using an Adenoviral Vector
US-226	A Phase II, Multi-Center, Open Label, Study to Evaluate Effectiveness and Safety of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 39 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)
US-228	Phase I Study of Concomitant Adenovirus-Mediated Transduction of Ovarian Cancer with HSV-tk Gene Followed by Intravenous Administration of Acyclovir and Chemotherapy with Topotecan in Patients after Optimal Debulking Surgery for Recurrent Ovarian Cancer
US-229	Neoadjuvant Pre-radical Prostatectomy Gene Therapy (HSV-tk Gene Transduction Followed by Ganciclovir) in Patients with Poor Prognostic Indicators
US-236	A Phase I Study of the Intraprostatic Injections of CN706, a Prostate-Specific Antigen Gene-Regulated Cytolytic Adenovirus, in Patients with Locally Recurrent Cancer Following Definitive Radiotherapy
US-238	Phase 1/2 Study of the Effects of Ascending Doses of Adenovirus Mediated Human FGF-4 Gene Transfer in Patients with Stable Exertional Angina
US-240	Phase I Trial of Adenoviral Vector Delivery of the Herpes Simplex Thymidine Kinase Gene by Intratumoral Injection Followed by Intravenous Ganciclovir in Patients with Advanced Non-Small Cell Lung Cancer

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Gene Therapy Clinical Trials Worldwide

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Displaying records **51** through **60** of **189** records found

Trial ID	Title
US-242	A Phase I Study of CD 154 Gene-Transduced Leukemia Cells in Patients with Chronic Lymphocytic Leukemia
US-243	Phase I Study of Direct Administration of a replication Deficient Adenovirus vector (AdGVVEGF121.10) Containing the VEGF121 cDNA to the Ischemic Lower Limb of Individuals with Peripheral Vascular Disease
US-248	Phase I Trial of Therapeutic Cancer Vaccine Using Intratumoral Injections of B7-1 (H5.030CMVhB7) in Patients with Metastatic Melanoma or Metastatic Breast Cancer
US-250	An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralesionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer
US-255	Phase I Trial of Intraperitoneal Adenoviral p53 Gene Therapy in Patients with Advanced Recurrent or Persistent Ovarian Cancer
US-256	Autologous, Irradiated, Melanoma Cells Transduced Ex Vivo with an Adenovirus Vector (Adv/GM-CSF) Expressing Granulocyte-Macrophage Colony Stimulating Factor Gene
US-257	Autologous, Irradiated, Cancer Cells (Breast Cancer, Colon Cancer, Head and Neck Cancer, and Soft Tissue Sarcoma) Transduced Ex Vivo with an Adenovirus Vector (Adv/GM-CSF) Expressing Granulocyte-Macrophage Colony Stimulating Factor Gene
US-258	Phase I Study of Direct Administration of a Replication Deficient Adenovirus Vector (AdGVVEGF121.10) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery DiseaseVia Minimally Invasive Surgery
US-262	A Phase I Study of Ad-p53 (NSC#683550) for Patients with Platinum- and Paclitaxel-Resistant Epithelial Ovarian Cancer
US-263	Phase I Trial of Adenovirus-Mediated Wild Type p53 Gene Therapy for Malignant Gliomas

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Trial ID	Title
US-267	A Phase I Study of Intralesional Administration of an Adenovirus Vector Expressing the HSV-1 Thymidine Kinase Gene (AdV.RSV-TK) in Combination with Escalating Doses of Ganciclovir in Patients with Cutaneous Metastatic Malignant Melanoma
US-268	Treatment of Patients with Stage IV Renal Cell Carcinoma with B7-1 Gene-Modified Autologous Tumor Cells and Systemic IL-2
US-269	A Phase I Trial Testing MART-1 Genetic Immunization in Malignant Melanoma
US-275	A Pharmacokinetic, Safety and Tolerability Study of Intravenous INGN in Patients with Advanced Cancer
US-276	Phase I Study of Ad-OC-TK Plus Valacyclovir for the Treatment of Metastatic or Recurrent Prostate Cancer
US-280	A Phase II/III Trial of Chemotherapy Alone Versus Chemotherapy Plus SCH 58500 in Newly Diagnosed Stage III Ovarian and Primary Peritoneal Cancer Patients with >0.5 cm and <2 cm Residual Disease Following Surgery
US-281	Phase I/II Trial of the Safety, Immunogenicity, and Efficacy of Autologous Dendritic Cells Transduced with Adenoviruses Encoding the MART-1 and gp100 Melanoma Antigens Administered With or Without Low Dose Recombinant Interleukin-2 (rIL-2) in Patients with Stage IV Melanoma
US-287	Phase I Pilot Trial of Adenovirus p53 in Bronchioloalveolar Cell Lung Carcinoma (BAC) Administered by Bronchoalveolar Lavage
US-288	Phase I Pilot Trial of Adenovirus p53 and Radiotherapy on Non-Small Cell Lung Cancer
US-296	Phase I Trial of Immunotherapy with Adenovirus-Interferon-Gamma (TG1041) in Patients with Malignant Melanoma

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Gene Therapy Clinical Trials Worldwide

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Trial ID	Title
US-304	Pediatric Phase I Study of AdV/RSV-TK Followed by Ganciclovir for Retinoblastoma
US-305	A Phase I Study of Infused Mobilized, Autologous Peripheral Blood Progenitor Cells, Which Have Been Incubated with a Recombinant Adenovirus-Wild-Type p53 Construct (SCH 58500) to Purge Any Contaminating Breast Cancer Cells, As Stem Cell Support After High-Dose Chemotherapy in Patients with Breast Cancer Metastatic to Bone and Bone Marrow
US-318	A Phase II Study of SCH 58500 in Combination with Chemotherapy Alone in Patients with Colorectal Cancer Metastatic to the Liver
US-319	Treatment of High Risk Acute Leukemia with CD40 Ligand and IL-2 Gene Modified Autologous Bone Marrow Fibroblasts and Tumor Cells
US-321	A Phase I Study of E1B-Attenuated Replication Competent Adenovirus Vector-Mediated Intratumoral Administration of the E. coli Cytosine Deaminase/HSV-1 Thymidine Kinase Fusion Gene in Conjunction with Two Prodrugs, 5-Fluorocytosine and Ganciclovir for Patients with Local Recurrence of Prostate Cancer after Radiation Therapy
US-324	Phase I-II Study Evaluating HSV-tk + Valacyclovir Gene Therapy in Combination with Radiotherapy for Prostate Cancer
US-325	Treatment of Recurrent or Progressive Malignant Glioma with a Recombinant Adenovirus Expressing Human Interferon-Beta (H5.010CMVhIFN-b): A Phase I Trial.
US-327	A Phase I Double-Blind, Placebo Controlled, Escalating Dose, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization
US-328	A Phase I, Open-Label, Multi-Center Extension Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization
US-329	A Phase I, Open-Label, Single Dose, Roll-Over, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization

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Trial ID	Title
US-334	A Phase I Study of FGF2-Fab' Modified Adenovirus Vector Mediated Intraperitoneal Delivery of Herpes Simplex Virus Thymidine Kinase (HSV-TK) Gene and Intravenous Ganciclovir in Previously Treated Ovarian and Extraovarian Patients
US-335	A Phase I Study of Vaccination with Lethally Irradiated, Autologous Ovarian Carcinoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor
US-338	A Tolerance and Efficacy Study of Neoadjuvant Intraprostatic GTx-001 Followed by Radical Prostatectomy in Patients with Locally Advanced Prostate Cancer
US-342	Phase I Trial tot Evaluate the Safety of H5.020CMVPDGF-B for the Treatment of a Diabetic Insensate Foot Ulcer
US-343	Phase I Trial to Evaluate the Safety of H5.020CMVPDGF-B and Limb Compression Bandage for the Treatment of Venous Leg Ulcer (Trial A)
US-344	A Phase I/II Dose Finding Trial of the Intraprostatic Injection of Calydon CV787, a Prostate-Specific Antigen Cytolytic Adenovirus, in Patients with Locally Recurrent Prostate Cancer Following Definitive Radiotherapy
US-345	A Phase I/II Dose Finding Trial of the Intravenous Injection of Calydon CV787, a Prostate-Specific Antigen Cytolytic Adenovirus, in Patients with Hormone Refractory Metastatic Prostate Cancer
US-346	A Phase II, Randomized, Multicenter, 26-Week Study to Assess the Efficacy and Safety of CI-1023 Delivered Through Minimally Invasive Surgery Versus Maximum Medical Treatment in Patients with Severe Angina, Advanced Coronary Artery Disease, and No Options for Revascularization.
US-347	Assessment of Direct Administration Via Minimally Invasive Surgery of a Replication Deficient Adenovirus Vector (AdCUVEGF.1) Containing the VEGF cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease
US-348	Assessment of Direct Administration Via Minimally Invasive Surgery of a Replication Deficient Adenovirus Vector (AdCUVEGF.1) Containing the VEGF cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease

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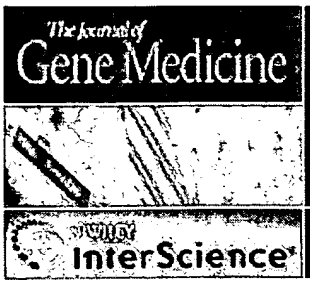

Gene Therapy Clinical Trials Worldwide

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Trial ID	Title
US-349	Effect of AdGVCFTR.10 on the Cystic Fibrosis Phenotype
US-358	Phase I Trial of Adenoviral Vector Delivery of the Human Interleukin-12 cDNA by Intratumoral Injection in Patients with Metastatic Breast Cancer to the Liver
US-359	Phase I Trial of Adenoviral Vector Delivery of the Human Interleukin-12 cDNA by Intratumoral Injection in Patients with Primary or Metastatic Malignant Tumors in the Liver
US-363	Phase I Study of the Replication-Competent, E1B-Attenuated Adenovirus with a CD/HSV-1 TK Fusion Gene and the Oral Administration of Valaciclovir in Adults with Penile Cancer
US-366	A Phase III Multi-Center, Open-Label, Randomized Study to Compare the Overall Survival and Safety off Bi-Weekly Intratumoral Administration of RPR/INGN 201 Versus Weekly Methotrexate in 240 Patients with Refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN)
US-369	A Phase I Study of Vaccination with Lethally Irradiated, Autologous Acute Myeloblastic Leukemia Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor in Patients with Advanced Myelodysplasia or Acute Myelogenous Leukemia
US-372	A Phase 1, Single-Dose, Dose-Escalation Study of MiniAdFVIII Vector in Patients with Severe Hemophilia A
US-374	A Phase I Open Label, Escalating Dose, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramyocardial Injection During Coronary Artery Bypass Grafting (CABG) Surgery in Patients with Areas of Viable and Underperfused Myocardium not Amenable to Bypass Grafting or Percutaneous Intervention and the related follow-up study A Phase I Open Label, Multi-Center Extension Study of Ad2/Hypoxia Inducible Factor (HIF)-1a/VP16 Gene Transfer Administered by Intramyocardial Injection During Coronary Artery Bypass Grafting (CABG) Surgery in Patients with Areas of Viable and Underperfused Myocardium not Amenable to Bypass Grafting or Percutaneous Intervention
US-379	Phase I Trial of Intradermal Adenovirus GA733 Vaccine for Advanced Colorectal Cancer
US-382	A Pilot Study of Gene Modified Autologous Neuroblastoma Vaccine for the Post-Chemotherapy Treatment of High Risk Neuroblastoma

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Gene Therapy Clinical Trials Worldwide

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Trial ID	Title
US-385	Phase I/II Study of GM-CSF Gene-Modified Autologous Tumor Vaccines in Early and Advanced Stage Non-Small Cell Lung Cancer (NSCLC)
US-386	Phase II Study of a B-7.1 Gene Modified Autologous Tumor Cell Vaccine and Systemic IL-2 for Patients with Stage IV Renal Cell Carcinoma.
US-387	A Randomized, Double-Blind, Placebo-Controlled, Multicenter, 12-Week Follow-up, Pilot Study of the Tolerability and Feasibility of Administering ADGVVEGF121.10 (CI-1023) Via the Biosense Intramyocardial Injection Device to Patients with Advanced Coronary Artery Disease
US-388	Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging, 26-Week Study to Assess the Safety and Efficacy of CI-1023 (ADGVVEGF121.10) in Peripheral Arterial Disease Patients with Severe, Disabling Intermittent Claudication
US-389	Phase I/IB Trial of Combination Adenoviral Vector Delivery of the Human Recombinant Interleukin-2 Gene and the Herpes Simplex Virus Thymidine Kinase Gene by Intratumoral Injection and Followed by Intravenous Ganciclovir in Patients with Hepatic Metastases from Colorectal Cancer
US-395	A Phase I/II Trial Investigating the Safety and Immunotherapy of Adenovirus Encoding the Melan-A/MART-1 and gp100 Melanoma Antigens Administered Intradermally to Patients with Stage II-IV Melanoma
US-397	A Feasibility Study of Catheter-Based Administration of a Replication Deficient Adenovirus Vector (AdCUVEGF.1) to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease
US-398	A Phase I Study of a Tropism Modified Adenovirus Vector for Intraperitoneal Delivery of Therapeutic Genes in Ovarian and Extraovarian Cancer Patients
US-399	An Open-Label, Phase I, Dose-Escalation Study of Tumor Necrosis Factor-alpha (TNFerade TM Biologic) Gene Therapy with Radiation Therapy for Locally Advanced, Recurrent, or Metastatic Solid Tumors
US-401	Phase II Study of Autologous Ad-CD154 Expressing Transduced CLL Cells in B Cell Chronic Lymphocytic Leukemia Patients Enrolled in Three Strata

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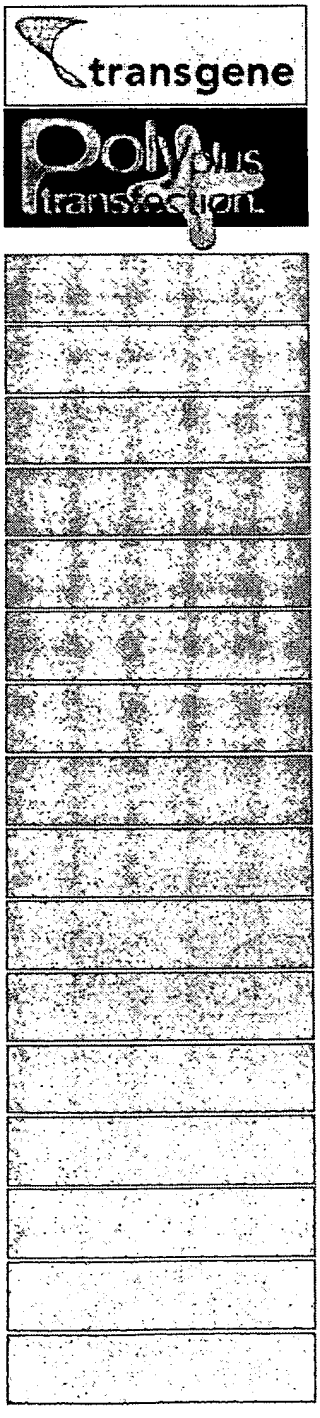

Gene Therapy Clinical Trials Worldwide

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Trial ID	Title
US-403	A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Effect of Ad5FGF-4 on Myocardial Perfusion Defect Size and Safety in Patients with Stable Angina
US-407	A Phase I, Double-blind, Placebo Controlled, Escalating Dose, Multi-center Study of Ad2/Hypoxia Inducible Factor (HIF)-1a /VP16 Gene Transfer Administration by Intramyocardial Injection During Coronary Artery Bypass Grafting (CABG) Surgery in Patients with Areas of Viable and Underperfused Myocardium not Amenable to Bypass Grafting or Percutaneous Intervention
US-412	A Phase III, Multi-Center, Open-Label, Randomized Study to Compare the Effectiveness and Safety of Intratumoral Administration of RPR/INGN 201 in Combination with Chemotherapy Versus Chemotherapy Alone in 288 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Sponsor: Aventis Pharmaceuticals - Gencell Division
US-414	A Phase I/II Trial Testing Alpha-Fetoprotein (AFP) Genetic Immunization in Hepatocellular Carcinoma.
US-418	A Randomized Phase II Study of Ad5CMV-p53 plus Radioactive Seed Implant vs Seed Implant Alone for PSA Relapse after External Beam Radiotherapy for Prostate Cancer. Sponsor: Introgen Therapeutics, Inc.
US-419	Intratumoral Injections of a Replication-Incompetent Adenoviral Vector Encoding a Factor VII Immunoconjugate to Induce a Cytolytic Immune Response against Melanoma Tumors: A Pilot Trial.
US-420	Phase I, Prospective, Placebo Controlled, Randomized Assessment of Direct Administration of a Replication Deficient Adenovirus Vector (AdCUVEGF121.1) Containing the VEGF121 cDNA to the Ischemic Myocardium of Individuals with Diffuse Coronary Artery Disease as an Adjunct to Coronary Bypass Surgery.
US-421	A Dose Escalating Phase I Study of AdPDGF-B/GAM in the Treatment of Diabetic Ulcers of the Lower Extremity. Sponsor: Selective Genetics, Inc.
US-426	A Phase I Study of Intratumoral Injections of OCaP1 for Metastatic or Locally Recurrent Prostate Cancer, Part 1: Dose Finding, Part 2: Index Lesion Escalation. Sponsor: DirectGene, Inc.
US-427	Effect of AdGVCFTR.10 on the Cystic Fibrosis Phenotype.

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Trial ID	Title
US-428	Phase I Study of Intraprostatic Administration of a Replication-Competent, Oncolytic Adenovirus Using Various Vector formulations to Patients with Localized Prostate Cancer Prior to Radical Prostatectomy.
US-430	A Phase I/II Trial Evaluating Intratumoral Injection of Interleukin-7 Gene Modified Autologous Dendritic Cells for the Treatment of Non-Small Cell Lung Cancer.
US-437	In Vivo Transfer of the CD40 Ligand Gene to Primary Lung Tumors to Activate Dendritic Cells and Induce Anti-Tumor Immunity.
US-439	Gene Therapy in Conjunction with Operative Bypass Grafting for Severe Peripheral Vascular Ischemia in Individuals with Insulin-Dependent Diabetes.
US-442	Phase I/II, Prospective Placebo Controlled, Randomized Assessment of Adenoviral Mediated VEGF121 cDNA Myocardial Angiogenesis Therapy as an Adjunct to Individuals with Diffuse Coronary Artery Disease Undergoing Off-Pump Coronary Artery Bypass Surgery.
US-445	Clinical Protocol for Wild Type p53 Gene Induction in Premalignancies of Squamous Epithelium of the Oral Cavity Via an Adenoviral Vector. Sponsor: Introgen Therapeutics, Inc.
US-447	Phase I Study of Adenovirus/PSA Vaccine in Men with Metastatic Prostate Cancer.
US-448	A Phase II/III, Multi-Center, Open-Label, Randomized Study to Compare the Effectiveness and Safety of Intralesional Administration of RPR/INGN 201 in Combination with Taxotere(R) and Carboplatin and Radiotherapy Versus Taxotere(R) and Carboplatin and Radiotherapy Alone in Patients with Locally Advanced Unresectable Non-Small Cell Lung Cancer (NSCLC). Sponsor: Introgen Therapeutics, Inc.
US-449	Phase I Study of Adenoviral Vector Delivery of the IL-12 Gene in Men with Local Recurrence of Prostate Cancer After Irradiation Therapy.
US-450	A Phase II Randomized Comparison Study of an Intraprostatic Injection of CV7606 Followed by External Beam Radiotherapy (EBRT) Versus EBRT Alone in Patients with Intermediate Risk, Clinically Localized Prostate Cancer. Sponsor: Calydon, Inc.

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Trial ID	Title
US-451	A Randomized, Placebo Controlled Phase II Study of an Intravenous Injection of CV787, a Prostate-Specific Antigen Oncolytic Adenovirus, Plus Weekly Docetaxel in Patients with Metastatic Hormone Refractory Prostate Cancer. Sponsor: Calydon, Inc.
US-452	A Multicenter, Randomized, Double-Blind, Placebo Controlled, Dose-Response Study to Evaluate the Efficacy and Safety of Ad5.1FGF-4 in Patients with Stable Angina. Sponsor: Berlex Laboratories.
US-453	A Multi-Center, Open Label, Two Part, Dose Escalation Study to Determine the Tolerability of Interferon-beta Gene Transfer in the Treatment of Recurrent or Progressive Glioblastoma Multiforme. Sponsor: Biogen.
US-454	Phase II Trial of Surgery with Perioperative RPR/INGN 201 (Ad5CMV-p53) Gene Therapy Followed by Chemoradiotherapy for Advanced Resectable Squamous Cell Carcinoma of the Oral Cavity and Oropharynx. Sponsor: Southwest Oncology Group.
US-455	Phase II, Single Arm, Single Institution Clinical Trial of Docetaxel and Doxorubicin in Combination with Local Administration of Ad5CMV-p53 (RPR/INGN-201) in Locally Advanced Breast Cancer (LABC). Sponsor: Introgen Therapeutics, Inc.
US-457	An Open-Label, Phase I, Dose-Escalation Study of TNFerade(TM) Biologic with Radiation Therapy as an Adjunct to Surgery or for Palliation of Soft Tissue Sarcoma of the Extremities. Sponsor: GenVec.
US-460	Treatment of High Risk Chronic Lymphocytic Leukemia (CLL) and Non-Hodgkin's Lymphoma (NHL) with IL-2 Gene Modified and CD40 Stimulated Autologous Tumor Cells.
US-464	Phase I Study of Combined Suicide Gene Therapy and Radiation Therapy for Locally Advanced Carcinoma of the Prostate.
US-470	A Phase I/II Dose Escalation and Activity Study of Intravenous Injections of OCaP1 in Subjects with Refractory Osteosarcoma Metastatic to Lung. Sponsor: DirectGene, Inc.
US-471	A Phase I/II Dose-Escalation Trial of Intratumoral Injection with a Replication-Deficient Adenovirus Vector, Ad-mda7 (INGN 241), in Combination with Radiation Therapy in Patients with Locally Recurrent Breast Cancer. Sponsor: Introgen Therapeutics, Inc.

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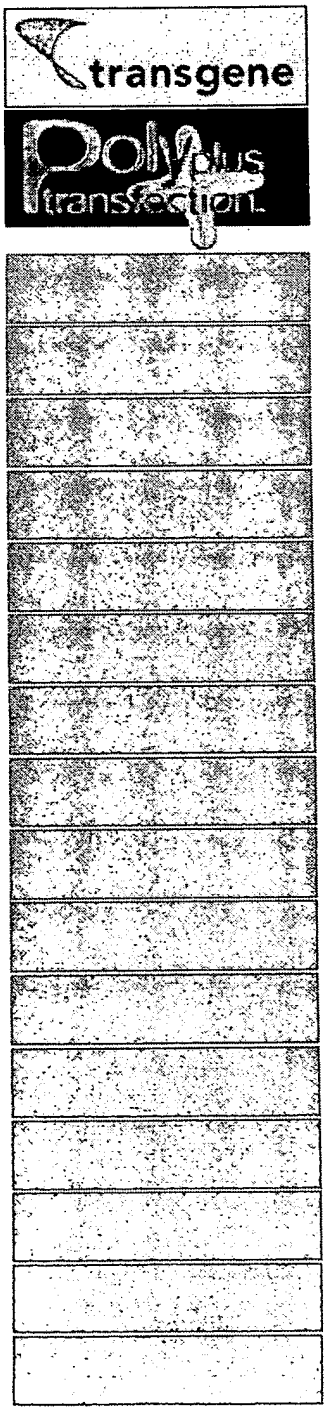

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Trial ID	Title
US-473	Administration of Neomycin Resistance Gene Marked LMP2A-Specific Cytotoxic T Lymphocytes to Patients with Relapsed EBV-Positive Hodgkin's Lymphoma
US-480	A Phase IIb, Randomized, Multicenter, Double-Blind Study of the Efficacy and Safety of TrinamTM (EG004) in Stenosis Prevention at the Graft-Vein Anastomosis Site in Dialysis Patient
US-485	Purging of Autologous Stem Cell Sources with bcl-xs Adenovirus for Women Undergoing High-Dose Chemotherapy for Stage IV Breast Carcinoma
US-487	An Open-Label, Phase I, Single Administration, Dose Escalation Study of ADGVPEDF.11D (ADPEDF) in Neovascular Age-Related Degeneration (AMD)
US-492	Clinical Trial of Adenoviral Vector Delivery of the Herpes Thymidine Kinase (HSV-TK) Gene by Intratumoral Injection Followed by Intravenous Ganciclovir with Imaging of HSV1-tk Gene Expression in Patients with Hepatic Metastases from Colorectal Cancer
US-499	Clinical Trial of Adenoviral Vector Delivery of the Herpes Thymidine Kinase (HSV-tk) Gene by Intratumoral Injection Followed by Intravenous Ganciclovir with Imaging of HSV-tk Gene Expression in Patients with Hepatic Metastases from Colorectal Cancer
US-500	Phase I Trial of Adenoviral Mediated Suicide Gene Therapy with HSV-tk Followed by Intravenous Administration of Ganciclovir in Patients with Locally Advanced and Refractory Superficial Bladder Cancer
US-509	A Phase I/II Trial of Intraprostatic Injection of CG7060 Followed by Three-Dimensional Conformal Radiation Therapy (3D-CRT) in Patients with Clinically Localized Intermediate or High-Risk Prostate Cancer
US-517	An Open Label, Dose-Escalation Study to Determine the Tolerability of Interferon-beta (BG00001) Gene Transfer in the Neoadjuvant Treatment of High-Risk Resectable Prostate Cancer
US-521	Inducible Nitric Oxide Synthase Gene Therapy for the Prevention of Intimal Hyperplasia in Arteriovenous Grafts used for Hemodialysis Access

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Trial ID	Title
US-530	A Randomized, Phase II, Study of TNFerade Biologic with 5-FU and Radiation Therapy for First-Line Treatment of Unresectable Locally Advanced Pancreatic Cancer
US-531	A Phase I Trial of Intrapleural Gene Therapy of Malignant Pleural Disease Using E1-Deleted Adenoviruses Containing the Human Interferon Beta Gene
US-532	Double-Blind, Randomized, Placebo-Controlled Study of Ascending Doses on Tolerability of Ad5.1 Mediated Human FGF-4 Gene Transfer Given Intramuscularly on One Day in Patients with Peripheral Arterial Occlusive Disease (PAOD) Fontaine Stage III or Fontaine Stage IV
US-533	Phase I Trial of In Situ Gene Therapy for Locally Recurrent Prostate Cancer Following Radiation Therapy Failure Using Sodium/Iodide Symporter and Radioiodine
US-534	Phase I Study of AD4-DeltaE3-HIV env and AD4-DeltaE3-HIV gag/pro Recombinant Vaccines in HIV-negative Volunteers
US-538	A Phase I-II Trial Using Dendritic Cells Transduced with an Adenoviral Vector Containing the p53 Gene to Immunize Patients with Extensive Stage Small Cell Lung Cancer after Standard Chemotherapy
US-542	AdV-tk Gene Therapy in Combination with Chemoradiation for Locally Advanced Pancreatic Cancer
US-549	A Phase II, Multi-Center, Single Arm Evaluation of Preoperative Chemoradiation Plus TNFeradeTM Biologic (AdGVEGR.TNF.11D) Prior to Esophagectomy for Locally Advanced Esophageal Cancer
US-556	Phase I Open-Label, Dose Escalation Trial Evaluating the Safety and Immunogenicity of Sequential Administration of Recombinant DNA and Adenovirus Expressing L523S Protein in Patients with Early Stage Non-Small Cell Lung Cancer
US-558	Adenovirus p53 Infected DC Vaccine for Breast Cancer

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Trial ID	Title
US-565	Study to Evaluate the Overall Response and Safety of Biweekly Intratumoral Administration of RPR/INGN 201 in Anaplastic Thyroid Cancer
US-571	A Phase II Randomized Study of GM-CSF Gene-Modified Autologous Tumor Vaccine (CG8123) With and Without Low-Dose Cyclophosphamide in Advanced Stage Non-Small Cell Lung Cancer
US-572	A Phase I/II Trial of Intraprostatic Injection of CG7870 Followed by Three-Dimensional Conformal Radiation Therapy (3D-CRT) in Patients with Clinically-Localized Intermediate-Risk Prostate Cancer
US-579	Virus Specific Cytotoxic T-Lymphocytes for the Prophylaxis of CMV after Allogeneic Stem Cell Transplant: A Dose Finding Trial
US-580	Phase II Study Examining the Biological Efficacy of Intratumoral INGN 241 (Ad-mda7) Administration in Patients with In Transit Melanoma
US-584	A Phase II Trial of Vaccination with Autologous Lethally Irradiated Melanoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Granulocyte-Macrophage Colony Stimulating Factor in Stage III and IV Metastatic Melanoma Patients
US-587	A Phase II Randomized Trial Concerning TNFerade Biologic with Capecitabine and Radiation Therapy followed by Surgical Resection Versus Capecitabine and Radiation Therapy followed by Surgical Resection for the Treatment of Rectal Cancer
US-589	A Phase 1 Study in Glaucoma Subjects Receiving SCH 412499 (rAd-p21) Administered as a Single Injection into the Subconjunctival Space Prior to Primary Trabeculectomy
US-590	Phase I/II Study of Replication-Competent Adenovirus-Mediated Double Suicide Gene Therapy in Combination with Conventional Dose Conformal Radiation Therapy for the Treatment of Intermediate to High-Risk Prostate Cancer
US-593	A Phase I Open-Label Safety Study of Intrastriatal Infusion of Adeno-Associated Virus Encoding Human Aromatic L-amino Acid Decarboxylase (AAV-hAAADC-2) in Subjects with Advanced Parkinson's Disease

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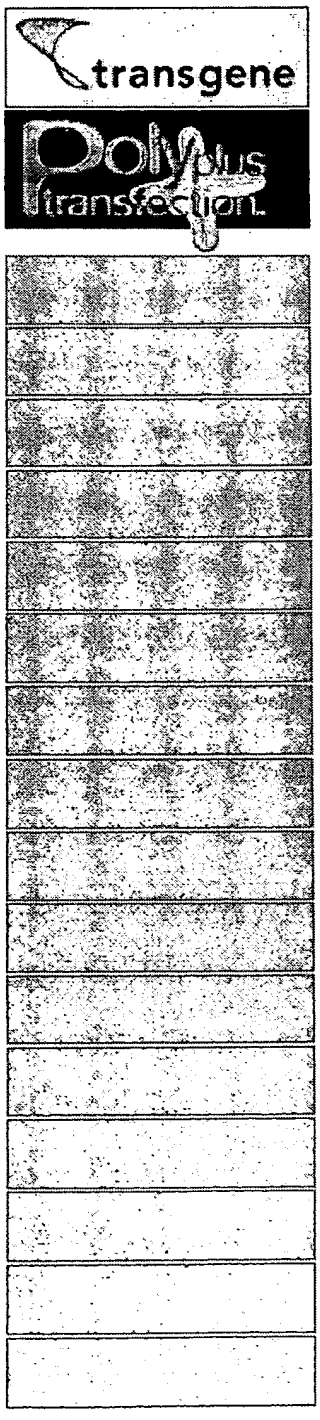

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Trial ID	Title
US-597	Phase I/II Study of Replication-Competent Adenovirus-Mediated Double Suicide Gene Therapy in Combination with Salvage Intensity Modulated Radiation Therapy for the Treatment of Locally Recurrent Prostate Cancer
US-598	Administration of Virus-Specific Cytotoxic T-Lymphocytes for the Prophylaxis and Therapy of Adenovirus Infection Post Allogeneic Stem Cell Transplant
US-601	Phase I Trial of Adenovirus-Mediated IL-12 Gene Transduction in Patients with Radiorecurrent Prostate Cancer
US-603	A Phase I Study of Ad5-TRAIL in Men with Clinically Organ Confined Prostate Cancer Undergoing Radical Prostatectomy
US-604	A Multinational Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Ad5FGF-4 in Patients with Stable Angina
US-608	Administration of LMP2A-Specific Cytotoxic T-Lymphocytes Following CD45 Antibody to Patients with Relapsed EBV-Positive Hodgkin's or Non-Hodgkin's Lymphoma
US-612	Phase II Trial of CG8123, an Autologous Cancer Vaccine (GVAX), in Patients with Selected Stage IIIB and IV Bronchioloalveolar Carcinoma (BAC)
US-620	A Phase I Study of Genetically Targeted Radiotherapy using Intratumoral Administration of Adenovirus Expressing the Sodium-Iodine Symporter (Ad-NIS) Plus Systemic 131I in Subjects with Refractory Squamous Cell Carcinoma of the Head and Neck
US-621	GM-CSF Secreting Leukemia Cell Vaccinations after Allogeneic Non-Myeloablative Peripheral Blood Stem Cell Transplantation in Patients with Advanced Myelodysplastic Syndrome or Refractory Acute Myeloid Leukemia
US-622	Adenylyl Cyclase VI Gene Transfer for CHF

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Trial ID	Title
US-624	Phase I Trial of Conditionally Replication-Competent Adenovirus (Delta-24-RGD) for Recurrent Malignant Gliomas
US-625	A Phase I Study of a Tropism Modified Conditionally Replicative Vector (Ad5-D24RGD) for Intraperitoneal Delivery in Ovarian and Extraovarian Cancer Patients
US-637	A Phase 1/2a Dose-Escalation Trial of Intravenous CG7870 in Combination with Docetaxel in Chemotherapy-Naïve Patients with Metastatic Hormone-Refractory Prostate Cancer
US-643	A Phase I/II Dose-Escalation Trial of Intravesical CG0070 for Superficial Transitional Cell Carcinoma of the Bladder after Bacillus Calmette-Guerin Failure
US-644	A Single Arm Open-Label Phase I Study of an Injectable Replication-Incompetent Adenoviral Vector Vaccine with Protein Boost Used to Produce an Immune Response for MUC-1 Positive Epithelial Cancer Cells in Advanced Breast Cancer Patients
US-660	A Single Arm Open-Label Phase I Study of an Injectable Replication-Incompetent Adenoviral Vector Vaccine with Protein Boost used to Produce an Immune Response for MUC-1 Positive Epithelial Cancer Cells in Prostate Cancer Patients
US-661	A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Dose-Selection Study of Ad2/Hypoxia Inducible Factor (HIP)-1 á/VP16 in Patients with Intermittent Claudication
US-666	A Phase I/II Study of Interferon-beta Gene Transfer (Ad.hIFN-â) in the Treatment of Refractory Colorectal Carcinoma with Liver Metastasis
US-668	Immunotherapy Consisting of Adenovirus Expressing P501 Protein Followed by CPC-P501 Protein Plus AS15 Adjuvant: A Phase I/II Trial of a Therapeutic Vaccine Regimen in Patients with Prostate Cancer who have PSA > 0.4 ng/ml after Radical Prostatectomy

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2000

PROGRAM/PROCEEDINGS

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Thirty-Sixth Annual Meeting

May 20–23, 2000
New Orleans, LA

*1807

A Phase II Trial of Adenoviral Mediated P53 Gene Transfer (RPR/INGN 201) in Conjunction with Radiation Therapy in Patients with Localized Non-Small Cell Lung Cancer (NSCLC). *S. Swisher, J. A. Roth, R. Komaki, M. Hicks, J. Ro, L. Dreiling, A. B. Yver, C. Stevens, J. B. Putnam, Jr., W. R. Smythe, A. A. Vaporciyan, G. L. Walsh; UT MD Anderson Cancer Ctr, Houston, TX; Rhone-Poulenc Rorer, Collegeville, PA*

We evaluated the efficacy of three intratumoral injections of adenoviral p53 (RPR/INGN 201) on days 1, 18 and 32 in conjunction with radiation therapy (60 gy) to treat 16 pts with localized NSCLC who were not candidates for surgery or chemoradiation. RPR/INGN 201 doses were escalated from 3×10^{11} to 3×10^{12} viral particles (vp) and were injected directly into the primary tumor by bronchoscopy (3 pts) or computed tomographic (CT) guidance (13 pts). 13 pts underwent 61 CT guided biopsies or injections with 13 pneumothoraces. These were managed with observation (8 pts) or percutaneous pleural catheter (5 pts). No treatment related mortality was observed. Grade 3 or 4 toxicity occurred in 3/16 (19%) patients. Tumor response was assessed by 3 month tumor biopsy and CT evaluation. Pathologic negative biopsies were noted in 8 out of 11 (62%) patients. Overall tumor response in the 13 evaluable patients was complete response 5 pts (39%), partial response 2 pts (15%), stable disease 1 pt (8%) and progression in 5 pts (39%). Median follow-up of all 16 pts was 7.2 months with a 1 yr survival of 65%. 1 year progression free survival was 45.5% (median, 8.0 months) with all failures occurring because of metastatic progression (5 pts) rather than local failure. These results suggest that adenoviral mediated p53 gene therapy can be safely accomplished in conjunction with radiation therapy. Compared to a previously reported 3 month pathologic control rate of 15 to 17% with chemoradiation or radiation therapy alone (LeChevalier et al., JNCI, 1991), the combination of RPR/INGN 201 and radiation therapy warrants further evaluation.

*1808

Downregulation of HER2, Induction of Apoptosis, and Increase in TNF-α Level After E1A Gene Therapy in Patients with Advanced Breast/Ovarian Cancers. *N. T. Ueno, W. Xia, S. Zhang, C. Bartholomeusz, J. K. Wolf, D. M. Gershenson, L. Huang, G. Lopez-Berestein, G. N. Hortobagyi, P. Anklesaria, M. Hung; M D Andeson Cancer Ctr, Houston, TX; Univ of Pittsburgh, Pittsburgh, PA; Targeted Genetics Corp, Seattle, WA*

E1A is recognized as a tumor suppressor gene by its repression of HER2 transcription, its repression of metastatic potential and induction of apoptosis in malignant cells, and its ability to prolong DFS in nude mice bearing HER2-overexpressing breast/ovarian cancers. We evaluated the molecular effect of an E1A-cationic liposome (DC-Chol) complex injected weekly into the thoracic or peritoneal cavities of pts with recurrent breast (n=6) or ovarian (n=6) cancers. In several pts, treatment resulted in stable disease (SD). Twelve tumor overexpressed HER2. We subjected tissue samples from 6 HER2-overexpressing pts' tumor to molecular analysis. In all 6 cases, this revealed E1A gene expression in both cancer and non-cancer cells and downregulation of HER2 expression via IHC (as confirmed by imaging analysis). In 5 of 6 cases, apoptosis was strongly induced (TUNEL assay). Because TNF-α induces apoptosis of E1A-transduced cells in vitro, TNF-α levels in intracavitary fluid were examined after E1A/DC-Chol injection, and a similar correlation was found. The precise mechanism behind these E1A's antitumor activities will be further evaluated in an upcoming Phase II trial of E1A gene therapy for ovarian cancer.

Pt no.	HER2 level	HER2 downregualtion	Apoptotis	No. of cells	TNF-α level	Clinical outcome
1	3+	60%	ND	-	↑	PD
2	3+	90-100%	↑↑↑	-	↑↑	SD
3	3+	45%	↑↑↑	-	↑↑	SD
4	2+	60%	↑↑	-	0	PD
5	2+	20%	↑	ND	0	ED
6	3+	90-100%	↑↑	-	↑↑	PD

PD: progression of disease, ED: early death, ND: not done.

*1809

Activity of E1A in Human Clinical Trials. *T. C. Reynolds, D. Alberts, D. Gershenson, L. Gleich, B. Glisson, E. Hanna, L. Huang, M. Hung, D. Kenady, N. Ueno, D. Villaret, G. Yoo; Targeted Genetics Corp, Seattle, WA; U of Arizona, Tucson, AZ; MD Anderson Cancer Ctr, Houston, TX; U of Cincinnati, Cincinnati, OH; U of Arkansas, Little Rock, AR; U of Pittsburgh, Pittsburgh, PA; U of Kentucky, Lexington, KY; U of Florida, Gainesville, FL; Wayne State Univ, Detroit, MI*

E1A has been shown to have potent anti-tumor activity in a number of model systems. Mechanistic studies have shown that E1A can: downregulate Her-2/neu expression, potentiate apoptosis, inhibit metastasis, and cause reversion of tumor cells toward a differentiated epithelial phenotype. In addition, in vitro and in vivo studies have shown that E1A can enhance the effects of both radiation and chemotherapeutic modalities. Phase I single agent studies in head and neck, breast, and ovarian cancer indicated that E1A was biologically active following local-regional administration using a DC-cholesterol/DOPE delivery vehicle. Progress in the evaluation of this agent in human clinical trials will be reviewed. Interim analysis of a Phase II trial of intratumoral administration of tgDCC-E1A in recurrent head and neck squamous cell carcinoma will be presented. A total of 24 patients were enrolled in the study. The study drug was well tolerated in all patients. CT imaging was used to objectively evaluate tumor response. The status of a Phase I study of chemotherapy in combination with tgDCC-E1A administration in patients with ovarian cancer. Finally, recent progress toward the development of a novel E1A formulation that is appropriate for intravenous delivery will be discussed.

*1810

Clinical Modulation of Gene Transcription Via Inhibition of Histone Deacetylase Using All-Trans Retinoic Acid Plus Sodium Phenylbutyrate. *L. H. Camacho, S. Novick, T. Tolentino, W. P. Tong, V. Richon, R. P. Warrell, Jr.; Memorial Sloan-Kettering Cancer Ctr, New York, NY*

Histone hyperacetylation promotes gene transcription in part by effecting chromatin relaxation. In APL and AML, the PML/RAR-α, PLZF/RAR-α, and AML1/ETO fusion proteins recruit SMRT/mSin3A/HDAC complexes that repress activation of their target genes. Moreover, recruitment of histone deacetylases (HDACs), and DNA hypermethylation, are recognized as general mechanisms of transcriptional repression in various solid tumors. We studied whether induction of histone hyperacetylation, coupled with a 'triggering agent', could induce gene activation and antitumor effects in human subjects. The study included 5 pts with APL, 2 with neuroblastoma, 2 with prostate cancer, 1 pt each with lung and head and neck cancer. All 11 pts received all-trans retinoic acid (RA) at doses from 30 to 90 mg/m2/day as the triggering agent, and sodium phenylbutyrate (PB), a known HDAC inhibitor, at doses from 200 to 400 mg/kg/day for 25 days. Serial Western analyses showed that PB reliably induced nuclear histone hyperacetylation in peripheral blood or marrow mononuclear cells. These effects were time-dependent; within 4–6 hrs after completing the PB infusion, histone acetylation returned to basal levels in most pts. A dose-response was observed in most pts. PB did not affect plasma concentrations of RA. Therapy was relatively well tolerated; major adverse reactions included transient CNS depression from PB, and RA-related effects were not exacerbated by PB. One pt with APL achieved a RT-PCR negative complete response sustained for 7 months over 5 treatment courses. One pt with neuroblastoma had stable disease during 2 courses, while all other pts failed to respond. We conclude that in vivo histone hyperacetylation can be safely and reproducibly induced in blood mononuclear cells. While this effect may be permissive, by itself it does not appear sufficient for activation of critical genes that are required to effect major antitumor responses in most pts. The identification of 'triggering agents' appropriate to other diseases, and drugs that effect DNA demethylation prior to introduction of HDAC inhibitors might also be required.